Stratton VA Medical Center
RESEARCH COMPLIANCE OFFICER
Standard Operating Procedure

I. FUNCTIONS

The Research Compliance Officer (RCO) will report directly to the Stratton VA Medical Center Director (MCD). The daily assignments and tasks will be independent of the research office. The RCO will perform the following functions:

- Conduct audits and reviews to ensure compliance with all VA and other federal requirements for the conduct of research, including (a) annual audits of all active studies to ensure that informed consent has been properly obtained and documented for each subject accrued since the previous audit, and (b) regulatory compliance audits for all active studies at least every 3 years.
- Serve as a local resource for regulations, policies, memoranda, alerts, and other VA and federal requirements related to research compliance.
- Serve as a non-voting member on the Institutional Review Board (IRB), Institutional Animal Care and Use Committee (IACUC), Subcommittee on Research Safety and Biosafety (SRS&B), and Research and Development (R&D) Committee.
- Provide education to investigators and research staff regarding regulatory and policy requirements.
- Provide education and guidance to the research oversight committees to enable the research staff to maintain a program that meets the objectives and requirements of the VHA handbooks and memorandums.
- Ensure prompt reporting in accordance with all applicable policies to the Office of Research Oversight (ORO).
- Promptly forward all auditing and monitoring reports in which any noncompliance is identified to the Facility Director and ORO, with simultaneous copies to the VISN Research Compliance Officer, Facility Chief of Staff (COS), Associate COS for Research (ACOS/R), Research and Development (R&D) Committee Chair, Institutional Review Board (IRB) Chair, and the Office of Research and Development (ORD), and where applicable, other external agencies such as OHRP, FDA, OLAW.

II. DEFINITIONS

Administrative Hold is a voluntary interruption of research enrollments and/or ongoing research activities by an appropriate facility official, investigator or sponsor. This does not apply to interruptions of research related to concerns regarding: safety, rights, or welfare of human research subjects, investigators, staff, or research animals.

Adverse Event any toward physical or psychological occurrence in a human subject participating in research.

Allegation of non-compliance is an assertion made by a party that must be proved or supported with evidence.

Animal (Laboratory Animal) is a live (non-human) vertebrate used or intended for use in research, research training, experimentation, or biological testing.

Continuing non-compliance is the persistent or repeated failure, either in the past or extending into the present, to comply with Federal regulations regarding research or the requirements and

determinations of the IRB, Human Research Protection Program (HRPP), or VHA Handbook 1200.05. Non-compliance applies to everyone, including: Investigators, Research Staff, or other persons associated with a research protocol, Committee Members, or Research Office.

Human Research is research involving any of the following: one or more human subjects, data containing identifiable private information about one or more living individuals, or one or more human biological specimens.

Principal Investigator is a qualified person designated by an applicant institution to direct a research project or program. The PI oversees scientific, technical and the day to day management of the research. The responsible leader.

Research is a systematic investigation designed to develop or contribute to generalizable knowledge.

Research Misconduct is defined as fabrication (making up data or results and recording or reporting them), falsification (manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record), or plagiarism (the appropriation of another person's ideas, processes, results, or words without giving appropriate credit) in proposing, performing, or reviewing research, or in reporting research results.

Serious non-compliance is the failure to adhere to the laws, regulations, or policies governing VA research that:

1. Results in substantive harm or damage (or risk of substantive harm or damage) to the safety, rights, or welfare of human subjects, research staff, or others; or
2. Results in substantive harm or damage (or risk of substantive harm or damage) to the safety or welfare of laboratory animals; or
3. Substantively compromise the integrity or effectiveness of research protections, either systemically or relative to a particular protocol or project.

Suspension or Termination of Research For purposes of this SOP:
Suspension refers to *temporary* interruption in the enrollment of new subjects or other ongoing research activities
Termination refers to a *permanent* halt in the enrollment of new subjects or other research activities
These terms apply to interruptions related to concerns regarding: safety, rights, or welfare of human subjects, investigators, staff, and laboratory animals.
These terms do not apply to interruptions resulting solely from the expiration of the IRB approval period.

Unanticipated or Unexpected Problem or AE is one that is unforeseen in terms of nature, severity, or frequency of occurrence, as documented in the protocol or other materials approved by the relevant oversight committees.

III. AUDIT PROCESS

The RCO conducts periodic auditing of the Stratton VA Medical Center's approved research to assess compliance with all applicable laws, regulations, and policies including those related to privacy, confidentiality, and information security requirements. Auditing is a mechanism to evaluate

VA's human subject research program and, when appropriate, identify areas for corrective action. An active auditing program should provide reasonable assurance of the integrity of the research program and that adequate protections for research subjects are in place. The RCO conducting the audits must be independent of the research program and the research study.

IV. AUDIT NOTIFICATION

A. "Not-for-Cause," Routine, Random, or Spot Audits

The RCO will randomly or systematically choose the protocol to audit and then notify the PI with an advanced notice of one to two weeks. The PI will choose from a choice of dates in this timeframe. This notification will be done via email to the PI and the coordinator, as applicable. If no response is received by the RCO within 3 business days, the RCO will then make a phone call to the PI. Once the date and time is determined, the RCO will send a confirmation letter stating the date, time, expected length of time needed for the visit and the list of items the RCO expects to review. Investigators may request to reschedule for appropriate reasons. Except in extreme circumstances, audits will not be postponed for more than 45 days after initial notification. If a response is not received within 30 days of the initial contact attempt, notification will be forwarded to the appropriate research subcommittee.

B. "For Cause" Audits

"For cause" audits will be scheduled within a few days of the audit request. Notification to PI and the coordinator, as applicable will be via e-mail (phone when required) to confirm a date and time for the audit. The Investigators must comply with the agreed upon date and time of the audit or notification will be forwarded to the IRB Committee. The PI or designated individual(s) may be present during the audit process. In instances where the PI chooses not to be present, a selected designee or someone associated with the project must be available for questions and answers that may arise during the audit. The PI is required to participate in an exit briefing at the completion of the audit or within 3 business days. A phone call exit briefing may be utilized in circumstances of scheduling conflicts.

C. Unannounced Audits

The RCO reserves the right to show up unannounced at any time to evaluate something specific.

V. FREQUENCY OF AUDITS

Beginning in FY2009, Veterans Health Administration (VHA) research facilities must conduct informed consent audits of all human research studies annually. Once subject enrollment of at least 1 human subject has begun, the study must be audited for compliance with the applicable regulations and policies related to research Informed Consents or Waiver of Consent at least once every year.

Beginning in FY2009, Veterans Health Administration (VHA) research facilities must conduct regulatory audits of all research studies at least once during the approval period and every 3 years.

The IRB, the study sponsor, the Principal Investigator (PI), VHA administration (ORD, ORO), Facility Director, the ACOS for R&D, or the RCO may require more frequent audits. They can also require

focused audits of 1 or more aspects of the study. The requirement to increase the frequency of audits or to audit specific aspects of the study can be based on such considerations as:

- Involvement of vulnerable populations
- Level of risk
- Phase I or Phase II studies
- Involvement of FDA approved drugs for which there has been a safety warning, or change in the labeling that indicates increased risks
- Issues of noncompliance
- Data breach

All compliance aspects of each study must be audited including PI's response to IRB requirements and the timeliness of the PI's response (based on IRB Minutes or other written documentation).

VI. AREAS TO BE AUDITED

Areas to be audited include, but are not limited to:

- Regulatory Compliance
- Study Staff Qualifications and Training
- Informed Consent (process and documentation)
- Waiver of informed consent
- Adverse event reporting and safety monitoring
- Inclusion and exclusion criteria
- Health Insurance Portability and Accountability Act of 1996 (HIPAA) compliant authorization
- Waiver of HIPAA compliant authorization and the required documentation by the IRB
- Compliance with all data security and data use requirements
- Compliance with all privacy and confidentiality requirements
- Protocol deviations
- Investigator Oversight

A. ANNUAL INFORMED CONSENT AUDITS

Beginning in FY2009, Veterans Health Administration (VHA) research facilities must conduct informed consent audits of all human research studies. The RCO will track all research studies to account for Exempt- Human, Exempt- Animal/Science, Waiver of signed ICD, Waiver of ICD or no consents obtained in the last 12 month reporting period. This allows the RCO to keep track of consent audits that did not involve an actual review of consent documents, recording the total number of audits done, regardless of whether or not it was necessary to review consent documents. At VA WNY Healthcare System all consents will be audited quarterly. A quarterly report will be reviewed with the convened IRB Committee. The informed consent audit report is included in the executive summary and forwarded to the MCD, the VISN RCO and the Compliance Advisory Board (CAB).

B. TRIENNIAL REGULATORY AUDITS

Beginning in FY2009, Veterans Health Administration (VHA) research facilities must conduct regulatory audits of all research studies (human, animal, and basic science) initiated after January 1, 2008 at least once during the approval period and every 3 years. A regulatory audit may be completed at the time of the study closure if not completed prior. A copy or a summary will be reviewed with the appropriate convened subcommittee. A summary of this report is included in the quarterly Executive Summary Report which is reviewed by the MCD and the VISN RCO. RCOs might plan that protocols are to be audited sooner if:

- The study will be closed or expire and has not been previously audited
- The study is determined to have greater than minimal risk
- The investigators has a previous history of serious or continuing noncompliance
- At the Research Oversight Committee request.

VIII. Non-Compliance

Serious or Continuing Noncompliance identified during a Research Compliance Officer's (RCO) audit must be reported as described in VHA Handbook 1058.01, *Requirements for Reporting Research Events to Facility Oversight Committees and the Office of Research Oversight*. An RCO identifying possible serious or continuing noncompliance (as defined in VHA Handbook 1058.01) during an informed consent or regulatory audit must report the noncompliance to the Facility Director, with additional notification of the Associate Chief of Staff for Research (ACOS/R), the Research and Development Committee (R&DC) Chair, and the Institutional Review Board (IRB) Chair within 5 business days of identifying it. The Facility Director has an additional 5 business days to report the noncompliance as identified by the RCO to the ORO Regional Office, the Office of Research and Development (ORD), and Veterans Integrated Service Network (VISN) leadership.

The following are ***examples*** of informed consent noncompliance that should be reported as described in the 5-day timelines above:

- Lack of a signed informed consent document for one or more subjects.
- Lack of signed Health Insurance Portability and Accountability Act (HIPAA) Research Authorization for one or more subjects.
- Repeated use of an unapproved, unstamped, or outdated informed consent document (an isolated case must still be reported to the IRB).
- Repeated failure to obtain dates of subjects signatures (an isolated case must still be reported to the IRB).
- Repeated failure to obtain the signature or signature dates of the witness or of the individual obtaining consent (an isolated case must still be reported to the IRB).

The following are ***examples*** of regulatory noncompliance that should be reported as described in the 5-day timelines above:

- Lack of IRB approval before initiating research.
- Initiating research procedures before obtaining consent.
- Initiating substantive protocol amendments without IRB approval, unless necessary to prevent immediate hazard to the subject.
- Failure of one or more members of the research team to satisfy the credentialing, privileging, or scope of practice requirements.
- Repeated failure to comply with IRB, R&DC, or other oversight committee determinations or requirements (an isolated case must still be reported to the IRB).
- Repeated failure to report AE's or problems with research per IRB and/or VA requirements (an isolated case must still be reported to the IRB).
- Repeated failure to maintain required study documents (an isolated case must still be reported to the IRB).

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VII. RCO REPORTING PROCESS & TIMEFRAMES

The RCO reports directly to the MCD and will work closely with the ACOS for R&D, AO for R&D, the research office staff and Committee Chairs. Weekly meetings with the Director will review areas of concern and accomplishments. The RCO will contact the MCD as needed with concerns or when reportable issues occur.

Informed consent audits and routine regulatory audits will be completed on an ongoing basis. A summary of these results will be included on the appropriate subcommittee agenda. The quarterly Executive Summary will include all audit reports which are reviewed by the MCD, the VISN RCO and the (CAB).

The RCO identifying possible serious or continuing non compliance will report an initial report to the MCD within five business days. A copy of this report will be submitted to the ACOS for R&D, R&D Chair and all pertinent subcommittee chairs. The MCD will submit a report of the possible non compliance, as identified by the RCO to Follow up reports will be provided as requested from ORO or ORD until resolution.

The Research Administrative Office will submit an annual Facility Directors Certification of Research Oversight. The RCO will complete the RCO Audit of VHA Research portion of the Certification checklist

- **Initial Report for Annual Informed Consent Audits:** The July 1, 2009, "Facility Director Certification of Research Oversight" will summarize informed consent audits for all studies active (open to enrollment or closed to enrollment but still with data collection or data analysis) at any time between January 1, 2009, and May 31, 2009. These audits will include review of all informed consent documents signed in the past 12 months prior to the audit, including "re-consents" or previously-enrolled subjects.

- **Subsequent Reports:** The July 1, 2010, "Facility Director Certification of Research Oversight" will summarize informed consent audits of all studies active at any time from June 1, 2009, through May 31, 2010, and will only include subjects accrued or "re-consented" since the previous audit. Subsequent certifications will summarize informed consent audits of all studies active at any time during the June 1 through May 31 reporting period.

- **Initial Report for Triennial Regulatory Audits:** The July 1, 2009, "Facility Director Certification of Research Oversight" will summarize regulatory audits conducted between January 1, 2009, and May 31, 2009. For this initial reporting period, regulatory audits are required only for human research studies that were initiated after January 1, 2008, and completed during the reporting period (i.e., completed between January 1 and May 31, 2009).

- **Subsequent Reports:** The July 1, 2010, Annual Facility Director Certification of Research Oversight will summarize regulatory audits from June 1, 2009, through May 31, 2010. Subsequent Annual Facility Director Certifications will summarize regulatory audits conducted during the June 1 through May 31 reporting period. Studies initiated after January 1, 2008 and completed within the June 1 through May 31 reporting period must receive a regulatory audit at closure or within 36 months preceding closure.

Investigators and other members of the VA research community including the RCO must report all problems involving, or suggesting, **risks to subjects or others** in VA research to the ACOS/R and the IRB Chair as soon as possible but no later than 5 business days after becoming aware of the problem. Such problems include, but are not limited to:

- Interruptions of subject enrollments or other research activities due to concerns about the safety, rights, or welfare of human research subjects, research staff, or others
- Any work-related injury to personnel involved in human research, or any research-related injury to any other person, requiring more than minor medical intervention or that leads to serious complications or death.
- Any VA National Pharmacy Benefits Management (PBM) Bulletins or Communications (sometimes referred to as PBM Safety Alerts) relevant to one or more of the facility's research projects.
- Any Data Monitoring Committee (DMC) report describing a safety problem.
- Any sponsor analysis describing a safety problem.

Investigators and other members of the VA research community including the RCO must report all problems involving, or suggesting, **research events related to research safety** in VA research to the ACOS/R and the IRB Chair as soon as possible but no later than 5 business days after becoming aware of the problem. Such problems include:

- Work-related and other injuries to personnel involved in VA research, or any research-related injury to any other person, requiring more than minor medical intervention or that leads to serious complications or death.
- Work-related exposures of VA research personnel to hazardous materials at greater than routine levels or that requires more than minor medical intervention or leads to serious complications or death.
- Any serious or continuing noncompliance with VA or other Federal requirements related to research safety (e.g., VHA Handbook 1200.06; VHA Handbook 1200.8; 7 CFR 331; 9 CFR 121; 29 CFR 1910 and 1960; and 42 CFR 72 and 73).
- Suspensions or terminations of ongoing research activities related to concerns regarding the safety, rights, or welfare of research staff or others.
- External noncompliance findings related to research safety by any VA office, any other Federal department or agency (e.g., United States Environmental Protection Agency), or any other entity (e.g., State Environmental Protection Agency).

Investigators and other members of the VA research community including the RCO must report all problems involving, or suggesting, **research information protection** in VA research to the ACOS/R and the IRB Chair as soon as possible but no later than 5 business days after becoming aware of the problem. Such problems include:

- Any serious or continuing research-related noncompliance with VA or other Federal requirements pertaining to information security or privacy (e.g., 45 CFR 160 and 164, VA Directive 6502, VA Handbook 6500, VHA Handbook 1605.1).
- Any unauthorized, research-related access, use, disclosure, transmission, removal, theft, or loss of VA sensitive information, including, but not limited to: protected health information, individually-identifiable private information (as defined in 38 CFR 16.102(f)(2)), confidential information and Privacy Act-protected information.

- Any research-related incidents reportable to the Office of Information and Technology (OI&T) Network and Security Operations Center (NSOC). ***NOTE:*** *Research personnel must adhere to all VA OI&T NSOC requirements, including those under which certain incidents be reported immediately. Research personnel must simultaneously provide such reports to the ACOS/R.*
- External noncompliance findings related to research information security or privacy by any VA office, any other Federal department or agency, or any other entity.

Any evidence of research misconduct uncovered during the course of an audit will be reported immediately to the Research Integrity Officer (RIO) and will be dealt with in accordance with VHA Handbook 1058.2 *Research Misconduct.*

IX. CORRECTIVE ACTIONS

The Stratton VA Medical Center Research Committees will determine appropriate corrective actions when regulatory deficiencies or procedural lapses are reported. The RCO does not have the authority to require remedial action. The committees may require corrective actions that include, but are not limited to:

1. Study termination
2. Approval suspension
3. Suspend enrollment and/or all or specific research procedures in the protocol in question
4. Mandated education for the PI and/or the research staff
5. A change in the reporting requirements (AEs, re-approvals, amendments, etc.). This change in reporting requirements may involve all studies under the direction of the PI, or only the particular study in which the deficiencies were identified
6. The establishment, by the PI, of a corrective action plan to ensure that deficiencies or lapses are corrected and do not re-occur.
7. Further monitoring of the research or consent process
8. Notification of current and past participants

Reporting of deficiencies and lapses to entities outside of the Stratton VA Medical Center will follow all established Federal, State, and VA regulations.

X. RCO Role in Education and Resources

The RCO will review new information received from meetings, conference calls or professional affiliations to research staff and committee members. Support will be provided to the research office staff for dissemination of information to the research investigators.

One on one training or support will be provided to the research investigators and staff as needed. This will include initial training on the informed consent process, documentation, maintaining research records and compliance with VA regulations.

The RCO will be familiar with the most current VHA Handbooks and Directives, FDA regulations, OLAW and Institutional Animal Care and Use Committee Guidebook, OHRP requirements,

References:

VHA Handbooks:
1200.05 Requirements for the Protection of Human Subjects in Research
1200.06 Control of Hazardous Agents in VA Research Labs
1605.1 Privacy and Release of Information
1200.08 Safety of Personnel Engaged in Research
1200.01 The Research and Development Committee Handbook
1058.01 Requirements for Reporting Research Events to Facility Oversight Committees and the Office of Research Oversight
1100.19 Credentialing and Privileging
1058.2 Research Misconduct
1200.7 Use of Animals in Research

VHA Directives:
2008-064 (Research Compliance Officers and the Auditing of VHA Human Subjects Research to Determine Compliance with Applicable Laws, Regulations, and Policies);
2008-6504 (Restrictions on Transmission, Transportation and Use of or Access to VA Data Outside VA Facilities);
2006-067 (Credentialing of Health Care Professionals);
2008-059 (Adverse Drug Event Reporting and Monitoring);
2008-002 (Disclosure of Adverse Events to Patients).

Code of Federal Regulations (CFRs):
Human Subjects Protection -**Title 38** (CFR), parts 16 and 17; **Title 45** CFR, parts 46 and 164; FDA - **21** CFR, parts 50, 54, 56, 312, 809, and 812.